APPENDIX B: EVIDENCE

5. Excerpt of the Handbook of Pharmaceutical Excipients

Handbook of Pharmaceutical Excipients

FIFTH EDITION

Edited by

Raymond C Rowe
BPharm, PhD, DSc, FRPharmS, CChem,
FRSC, CPhys, MInstP

Chief Scientist
Intelligensys Ltd
Billingham, UK

Paul J Sheskey
BSc, RPh

Technical Services Leader
The Dow Chemical Company
Midland
MI, USA

Siân C Owen
BSc, MA

Development Editor
Royal Pharmaceutical Society of Great Britain
London, UK

APhA

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Mannitol

1 Nonproprietary Names

BP: Mannitol
JP: D-Mannitol
PhEur: Mannitolum
USP: Mannitol

2 Synonyms

Cordycepic acid; C*PharmMannidex; E421; manna sugar; D-mannite; mannite; *Mannogem*; *Pearlitol*.

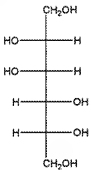
3 Chemical Name and CAS Registry Number

D-Mannitol [69-65-8]

4 Empirical Formula and Molecular Weight

$C_6H_{14}O_6$ 182.17

5 Structural Formula



6 Functional Category

Diluent; diluent for lyphilized preparations; sweetening agent; tablet and capsule diluent; tonicity agent.

7 Applications in Pharmaceutical Formulation or Technology

Mannitol is widely used in pharmaceutical formulations and food products. In pharmaceutical preparations it is primarily used as a diluent (10–90% w/w) in tablet formulations, where it is of particular value since it is not hygroscopic and may thus be used with moisture-sensitive active ingredients.[1,2]

Mannitol may be used in direct-compression tablet applications,[3–7] for which the granular and spray-dried forms are available, or in wet granulations.[8] Granulations containing mannitol have the advantage of being dried easily. Specific tablet applications include antacid preparations, glyceryl trinitrate tablets, and vitamin preparations. Mannitol is commonly used as an excipient in the manufacture of chewable tablet formulations because of its negative heat of solution, sweetness, and 'mouth feel'.[9,10]

In lyophilized preparations, mannitol (20–90% w/w) has been included as a carrier to produce a stiff, homogeneous cake that improves the appearance of the lyophilized plug in a vial.[11–20] A pyrogen-free form is available specifically for this use.

Mannitol has also been used to prevent thickening in aqueous antacid suspensions of aluminum hydroxide (<7% w/v). It has been suggested as a plasticizer in soft-gelatin capsules, as a component of sustained-release tablet formulations,[21] and as a carrier in dry powder inhalers.[22,23] It is also used as a diluent in rapidly dispersing oral dosage forms.[24,25] It is used in food applications as a bulking agent.

Therapeutically, mannitol administered parenterally is used as an osmotic diuretic, as a diagnostic agent for kidney function, as an adjunct in the treatment of acute renal failure, and as an agent to reduce intracranial pressure, treat cerebral edema, and reduce intraocular pressure. Given orally, mannitol is not absorbed significantly from the GI tract, but in large doses it can cause osmotic diarrhea; *see* Section 14.

8 Description

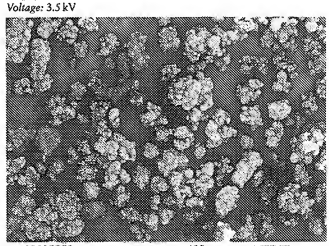
Mannitol is D-mannitol. It is a hexahydric alcohol related to mannose and is isomeric with sorbitol.

Mannitol occurs as a white, odorless, crystalline powder, or free-flowing granules. It has a sweet taste, approximately as sweet as glucose and half as sweet as sucrose, and imparts a cooling sensation in the mouth. Microscopically, it appears as orthorhombic needles when crystallized from alcohol. Mannitol shows polymorphism.[26]

9 Pharmacopeial Specifications

See Table I.

SEM: 1
Excipient: Mannitol
Manufacturer: Merck
Magnification: 50×
Voltage: 3.5 kV



Sodium Lauryl Sulfate

1 Nonproprietary Names

BP: Sodium lauryl sulfate
JP: Sodium lauryl sulfate
PhEur: Natrii laurilsulfas
USPNF: Sodium lauryl sulfate

2 Synonyms

Dodecyl sodium sulfate; *Elfan 240*; sodium dodecyl sulfate; sodium laurilsulfate; sodium monododecyl sulfate; sodium monolauryl sulfate; *Texapon K12P*.

3 Chemical Name and CAS Registry Number

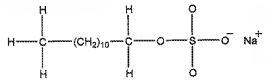
Sulfuric acid monododecyl ester sodium salt [151-21-3]

4 Empirical Formula and Molecular Weight

$C_{12}H_{25}NaO_4S$ 288.38

The USPNF 23 describes sodium lauryl sulfate as a mixture of sodium alkyl sulfates consisting chiefly of sodium lauryl sulfate ($C_{12}H_{25}NaO_4S$). The PhEur 2005 states that sodium lauryl sulfate should contain not less than 85% of sodium alkyl sulfates calculated as $C_{12}H_{25}NaO_4S$.

5 Structural Formula



6 Functional Category

Anionic surfactant; detergent; emulsifying agent; skin penetrant; tablet and capsule lubricant; wetting agent.

7 Applications in Pharmaceutical Formulation or Technology

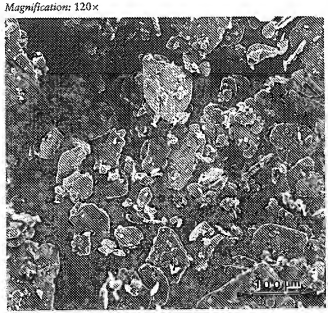
Sodium lauryl sulfate is an anionic surfactant employed in a wide range of nonparenteral pharmaceutical formulations and cosmetics; *see* Table I.

It is a detergent and wetting agent effective in both alkaline and acidic conditions. In recent years it has found application in analytical electrophoretic techniques: SDS (sodium dodecyl sulfate) polyacrylamide gel electrophoresis is one of the more widely used techniques for the analysis of proteins;[1] and sodium lauryl sulfate has been used to enhance the selectivity of micellar electrokinetic chromatography (MEKC).[2]

Table I: Uses of sodium lauryl sulfate.

Use	Concentration (%)
Anionic emulsifier, forms self-emulsifying bases with fatty alcohols	0.5–2.5
Detergent in medicated shampoos	≈10
Skin cleanser in topical applications	1
Solubilizer in concentrations greater than critical micelle concentration	>0.0025
Tablet lubricant	1.0–2.0
Wetting agent in dentrifices	1.0–2.0

SEM: 1
Excipient: Sodium lauryl sulfate
Manufacturer: Canadian Alcolac Ltd.
Magnification: 120×



8 Description

Sodium lauryl sulfate consists of white or cream to pale yellow-colored crystals, flakes, or powder having a smooth feel, a soapy, bitter taste, and a faint odor of fatty substances.

9 Pharmacopeial Specifications

See Table II.

10 Typical Properties

Acidity/alkalinity: pH = 7.0–9.5 (1% w/v aqueous solution)
Acid value: 0
Antimicrobial activity: sodium lauryl sulfate has some bacteriostatic action against Gram-positive bacteria but is